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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,794	04/08/2005	Francis Thomas Boyle	100864-1P US	4278

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ASTRAZENECA R&D BOSTON
35 GATEHOUSE DRIVE
WALTHAM, MA 02451-1215

EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,794	BOYLE ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,7,15,17-19 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,17-19 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is office action is in response to applicant's request for continued examination filed on April 17, 2009.

Continued Examination under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Status of claims

Amendment of claims 7, 15, and 19; and cancellation of claims 10, 12-14, 16, 20-22 and 24 is acknowledged.

Claims 1-4, 6-7, 15, 17-19 and 23 are pending and are the subject of this office action.

Claims 1-4, 6-7, 15, 17-19 and 23 are presently under examination.

The following species are being examined: ZD4054 (Zibotentan) as the endothelin receptor antagonist, and ZD1839 (Iressa-Gefitinib) as the EGFR TKI.

Priority

The present application claims priority to application No. PCT/GB03/04347 filed 10/07/2003, which claims priority to foreign application No. UNITED KINGDOM 0223854.1 filed on 10/12/2002.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103 (New Rejection Necessitated by Amendment).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6-7, 15, 17-19 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fujimura et. al. (Clinical Cancer Research (July 2002) 8:2448-2454), Salani et. al. (Clinical Science (August 2002) 103 (Suppl. 48) 318S-321S), and Bradbury et. al. (US 6,258,817).

Claims 1-4 and 17 recite a combination comprising ZD1839 (Iressa-Gefitinib, species elected as the EGFR TKI) and ZD4054 (Zibotentan, species elected as the endothelin receptor antagonist).

For claims 1-4 and 17 Fujimura teaches a composition comprising ZD1839 for the treatment of ovarian cancer (see title and abstract).

Fujimura does not teach a composition comprising ZD4054 for the treatment of ovarian cancer. However, Salani teaches that endothelin receptor antagonists (e.g. ABT-627) are effective in the treatment of ovarian cancer and Bradbury teaches that ZD4054 is an endothelin receptor antagonist (see abstract and column 63, lines 34-35).

At the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to combine two compositions (ZD1839 and ABT-627) each of which is taught by the prior art to be useful for the same purpose (treating ovarian cancer), in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). And, Since Salani teaches that ABT-627 is an endothelin receptor antagonist, and since Bradbury teaches that ZD4054 is an endothelin receptor antagonist, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (ABT-627 or any endothelin receptor antagonist) for another (ZD4054) with an expectation of

success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claims 1-4 and 17 with a reasonable expectation of success.

Claim 6 further limits claim 1, wherein the composition further comprises a pharmaceutically acceptable diluent or carrier.

Claim 18 further limits claim 17, wherein the composition further comprises a pharmaceutically acceptable diluent or carrier.

For claims 6 and 18, Bradbury further teaches that the pharmaceutical compositions comprising endothelin receptor antagonists further comprise pharmaceutically acceptable carriers (see column 17, lines 29-43).

Claims 7 and 19 recite a method of treating ovarian cancer, in a warm blooded animal such as man, in need of such a treatment which comprises administering to said animal an effective amount of a combination comprising ZD1839 (Iressa-Gefitinib, species elected as the EGFR TKI) and ZD4054 (Zibotentan, species elected as the endothelin receptor antagonist).

For claims 7 and 19 Fujimura teaches a method of treating ovarian cancer comprising administering ZD1839 (see title and abstract).

Fujimura does not teach a method of treating ovarian cancer comprising ZD4054. However, Salani teaches that endothelin receptor antagonists (e.g. ABT-627) are effective in the treatment of ovarian cancer and Bradbury teaches that ZD4054 is an endothelin receptor antagonist (see abstract and column 63, lines 34-35).

At the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to treat ovarian cancer combining two compositions (ZD1839 and ABT-627) each of which is taught by the prior art to be useful for the same purpose (treating ovarian cancer cancer), in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (see MPEP 2144.06). *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). And since Salani teaches a method of treating ovarian cancer with an endothelin receptor antagonist, and since Bradbury teaches that ZD4054 is an endothelin receptor antagonist, at the time of the invention it would have been *prima facie* obvious for a person of ordinary skill in the art to substitute one functional equivalence (any endothelin receptor antagonist) for another (ZD4054) with an expectation of success, since the prior art establishes that both function in similar manner, thus resulting in the practice of claims 7 and 19, with a reasonable expectation of success.

Claim 15 further limits claim 7, wherein the cancer is in a non-metastatic state.

Claim 23 further limits claim 19, wherein the cancer is in a non-metastatic state.

For claims 15 and 23, neither Fujimura nor Salani mention that the ovarian cancer is in a metastatic state, so it is safe to assume that the ovarian cancer they are treating is in a non-metastatic state. Also, even though they are silent whether the ovarian cancer is in a metastatic or non-metastatic state, at the time of the invention, it would have been prima facie obvious for the skilled in the art to treat metastatic or non-

metastatic ovarian cancer since both Fujimura and Salani teach the treatment of ovarian cancer in general, thus resulting in the practice of claims 15 and 23, with a reasonable expectation of success.

Withdrawn Rejections and/or Objections

Claims rejected under 35 USC 112 first paragraph (enablement)

Due to applicant amendment of claims 7 and 19, the enablement rejection is now moot.

Rejection under 35 USC 112 first paragraph is withdrawn.

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
June 24, 2009

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642